DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service

Food and Drug Administration
1141 Central Parkway
Cincinnati, OH 45202-1097

December 18, 1997

WARNING LETTER
CIN-WR-98-90

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Gary Lewis, President
American Air Gases
9045 Osborne Drive
Mentor, OH 44060

Dear Mr. Lewis:

On November 10-12, 1997, an inspection was conducted of your medical gas facility, at the above address, covering your transfilling of Oxygen USP and Nitrogen NF compressed gases, liquid Oxygen USP in large cryogenic vessels, and the manufacture of Medical Air USP. During this inspection, our investigator documented serious deviations from the Current Good Manufacturing Practices Regulations (Title 21 Code of Federal Regulations, Part 211). These deviations cause your drug products, Oxygen USP, Medical Air USP, and Nitrogen NF to be adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act).

Furthermore, the inspection documented your medical gases Oxygen USP, Nitrogen NF and Medical Air USP are misbranded under section 503(b)(4) of the Act in that they are prescription drugs, being distributed for other than emergency use, and they fail to bear the statement "Caution: Federal law prohibits dispensing without prescription".

Specific observations made during the Inspection include:

(1) Failure to test incoming Oxygen USP liquid and Nitrogen NF liquid.

FDA requires that all USP/NF tests, where appropriate, be performed on incoming medical gases and finished product. Since you fill Oxygen USP into large cryogenic vessels (L-180 Dewars), and mix Nitrogen NF and Oxygen (Medical Air USP), your firm must sample and test both of these incoming bulk gases (Oxygen USP and Nitrogen NF) directly from the stand tanks, immediately after each delivery.

(2) Batch production records for compressed medical gases are incomplete and inadequate in that they lack prefill, fill and post fill checks.

See the attached document "Fresh Air 97" for an example batch record and descriptions of these tests. In addition to the tests shown on the example batch record, systems utilizing control panels to distribute different gases from multiple storage tanks, as in your case, have a requirement for documentation of additional testing or verification.

For control panel systems connected to multiple gas stand tanks, controls must be in place to assure that only the proper gases are added to the finished product cylinders. This can be done by either of two methods. You may either test each lot of finished product for each of the gases connected to the control panel or you may implement an additional (second) visual verification check.

If the second check is used, the batch production records must include documentation of the visual check by a second person other than the operator, such documentation would include initials of the second individual to verify that a visual exam has been done to assure that the proper gases are added to the cylinders each time the control panel connections are changed, ie. for mixtures such as Medical Air USP addition of both the Nitrogen and Oxygen would be verified separately.

(3) Lack of written operating procedures describing: (a) the receipt and acceptance of incoming liquid medical; (b) transfilling production and control procedures, including procedures for controlling access and use of adapters in manufacture of medical gas mixtures; (c) testing of finished medical gases; (d) calibration of analytical equipment (oxygen analyzer and Gas Chromatograph), pressure gauges, vacuum gauges; (e) employee training; (f) label issuance; and (g) handling of recalls and complaints.

(4) Failure to adequately test Nitrogen NF containing drug products in that neither the supplier's certificate of analysis nor the finished drug product testing includes the required USP/NF test for Carbon Monoxide.

For Nitrogen NF drug products, you must either perform full USP testing (including Carbon Monoxide) on the incoming gas, or receive the liquid gas under a suppliers certificate of analysis, which includes test results for Carbon Monoxide. Review of your supplier's certificate of analysis (COA) for Nitrogen NF batch NO2070997-A, trailer 3167, reveals no entry for the Carbon Monoxide test results, also this particular COA was not dated to provide a record of the date of delivery.

The above described violations are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure that you adhere to all current regulations applicable to your operations. Until these violations are corrected, Federal agencies will be informed that FDA recommends against award of contracts for affected products.

You should take prompt action to correct these violations. Failure to achieve prompt correction may result in regulatory action without further notice. These include seizure and/or injunction.

Please advise us in writing within fifteen (15) working days of receipt of this letter of the specific actions you are taking to correct these violations. Your response should explain each step you have taken to correct the noted violations, including steps taken to prevent recurrence of similar violations. Include any documentation showing these corrections. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your reply should be sent to the U.S. Food and Drug Administration, 1141 Central Parkway, Cincinnati, Ohio 45202-1097, to the attention of Charles S. Price, Compliance Officer. Any questions regarding this letter may be directed to Mr. Price at telephone (513) 684-3501 extension 165.

For your information, to assist you in complying with FDA regulations, I have enclosed copies of the FDA "Compressed Medical Gases Guideline" and the FDA speech, FRESH AIR 97 - A LOOK AT FDA'S MEDICAL GAS REQUIREMENTS. These describe current FDA requirements and policy on medical gases.

Sincerely,

Diana J. Kolaitis
District Director
Cincinnati District

Enclosures: Fresh Air "97"
Compressed Medical Gases Guideline